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# (12) United States Patent

Nagy et al.

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#### (54) INHIBITION OF SELECTIN BINDING

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#### Related U.S. Application Data

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- (60) Provisional application No. 60/012,894, filed on Mar. 1, 1996.

### (56) References Cited

### U.S. PATENT DOCUMENTS

5,470,843	*	11/1995	Heavner et al. 530/329 Stahl et al. 514/61 Ward et al. 514/460
5,489,578	*	2/1996	Rosen et al 514/61
5,508,387		4/1996	Tang et al
5,510,481		4/1996	Bednarski et al
5,512,294	帧	4/1996	Li et al 424/450
5,576,305	*	11/1996	Ratcliffe 514/25

#### OTHER PUBLICATIONS

Wilson Et Al., Polydiacetylene Monolayers Functionalized with Amino Acids, Langmuir, 1992, pp. 2361–2364, vol. 8, No. 10.

Yamazaki Et Al., Studies on Carbohydrate–Binding Proteins Using Liposome–Based Systems–I. Preparation of Neoglycoprotein–Conjugated Liposomes and Feasability of their Use as Drug–Tergeting Devices, Int. J. Biochem, 1992, pp. 99–104, vol. 24, No. 1.

Yamazaki Et Al., Neoglycoprotein–Liposomes and lectin–Liposome Conjugates as Tools for Carbohydrate Recognition Research, Methods in Enzymology, 1994, pp. 56–65, vol. 242.

Murohara Et Al., Cardioprotection by liposome–conjugated sialy Lewis–oligosaccharide in myocardial ischemia and reerfusion injury, Cardiovascular Research, 1995, pp. 965–974, vol. 30.

O'Brien Et Al., Preparation and Characterization of Polymerized Liposomes, Annals New York Academy of Sciences, pp. 282–295 (1985).

Papahadjopoulos Et Al., Sterically stabilized liposomes: Improvements in pharmacokinetics and antitumor therapeutic efficacy, Proc. Natl. Acad. Sci., 1991, pp. 11460–11464, vol. 88.

Charych Et Al., Direct Colorimetric Detection of a Receptor–Ligand Interaction by a Polymerized Bilayer Assembly, Science, 1993, pp. 585–588, vol. 261.

Spevak Et Al., Chapter 4. Biological Applications of Ligands Presented on the Surface of Polymerized Liposomes, The Presentation of Biological Ligands on the Surface of Polymerized Monolayers and Liposomes, 1993, pp. 110–122.

Spevak Et Al., Molecular Assemblies of Functionalized Polydiacetylenes, Advanced Materials, 1995, pp. 85–89, No. 1

Spevak Et Al., Polymerized Liposomes Containing C-Glycosides of Sialic Acid: Potent Inhibitors of Influenza Virus in Vitro Infectivity, J. Am. Chem. Soc., 1993, pp. 1146–1147, No. 115.

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## (57) ABSTRACT

This invention provides compositions for inhibiting the binding between two cells, one expressing P- or L-selectin on the surface and the other expressing the corresponding ligand. A covalently crosslinked lipid composition is prepared having saccharides and acidic group on separate lipids. The composition is then interposed between the cells so as to inhibit binding. Inhibition can be achieved at an effective oligosaccharide concentration as low as 10<sup>6</sup> fold below that of the free saccharide. Since selectins are involved in recruiting cells to sites of injury, these composition scan be used to palliate certain inflammatory and immunological conditions.

### 12 Claims, 8 Drawing Sheets

<sup>\*</sup> cited by examiner